Gastrointestinal adaptation to diets of differing fat composition in human volunteers

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Abstract

The effect of a low fat diet (9 MJ) *v* a high fat diet (19·26 MJ), each consumed separately for four and 14 days, on gastric emptying and mouth to caecum transit time of a high fat test meal and body weight and satiety were examined in groups of 10 and six normal male volunteers. The half time for gastric emptying ($t^1/_2$) and the mouth to caecum transit time of a high fat test meal was significantly faster after the high fat diet than the low fat diet when consumed for 14 days ($t^1/_2$=98 (80–116) *v* 147 (88–206) minutes (median (range)), p<0·05; mouth to caecum transit time 240 (130–350) *v* 360 (200–520) minutes, p<0·05), but not when consumed for only four days. The mean (SEM) body weight of all subjects significantly increased during the 14 day high fat diet (74·7 (1·3) *v* 72·7 (1·6) kg, p<0·05) but was not influenced during the consumption of the low fat diet. When subjects were given an appetising meal to consume on the day that they had consumed the transit test meal, they ate similar amounts irrespective of their recent dietary history, though the eating rate was significantly slower after the high fat diet (mean (SEM)) 46·7 (1·9) *v* 71·3 (14·8)/min, p<0·05). Maintaining normal subjects on a high or low fat diet for two weeks resulted in a desensitisation or sensitisation respectively of the mechanisms by which nutrients regulate gastrointestinal transit. These findings emphasise the importance of the recent dietary history in the interpretation of gastric emptying and small bowel transit time data.

The presence of nutrients, such as glucose[1,2] and fat,[3,4] in the small intestine exert a powerful inhibitory effect on the rate of gastric emptying, but it is possible that this effect may be modulated by previous dietary history. Gastric emptying of nutrient liquids is delayed in primary anorexia nervosa[5–8] and after a period of starvation, [9,10] but returns to control values after a two week refeeding programme.[7,8] In contrast, some, but not all, studies have shown an acceleration in the rate of emptying of nutrient liquids[11,12] in obese patients. These results suggest that underexposure or overexposure of the small intestinal receptors to nutrients may alter the sensitivity of the mechanisms that regulate gastric emptying. This hypothesis is supported by the observation that the emptying of weak acids from the stomach is faster in subjects with hypochlorhydria[13,14] than in normal subjects and by our recent results showing that supplementation of the diet of healthy volunteers with 400 g glucose per day for three days accelerated the emptying of a hyperosmotic drink of glucose from the stomach (unpublished data). If our hypothesis is correct then it is likely that small bowel transit time and eating behaviour, both of which are also modulated by the nutrient content of the diet,[2] should also be influenced by dietary history.

The aim of these experiments was to investigate whether the gastrointestinal responses to fat can be modulated by previous fat intake.

Methods

Studies were carried out on 12 healthy male volunteers aged 19–29 years. None of the subjects had taken any medication or suffered recent gastrointestinal upset before the studies. The weights of all subjects were in the normal range for their age and height. Each gave written informed consent for the studies to be performed. The protocols were approved by the Southern District Ethical Committee of the Sheffield Area Health Authority (Teaching) (July 1987).

PROTOCOL

Paired measurements of gastric emptying and mouth to caecum transit time of a high fat meal was carried out after healthy male subjects had consumed diets with either high or low fat contents for consecutive and randomised periods of either four days (n=10) or 14 days (n=6). Body weight was monitored during the 14 day studies and a satiety test was carried out at the end of the day on which transit was measured.

DIETS

The low fat and high fat diets were carefully chosen to contain identical amounts of protein and carbohydrate, but appreciably different amounts of fat and total calories[15] (Table I). The design of the high fat diet was essentially similar to that of the low fat diet except that skimmed milk was replaced with full cream milk and butter and mayonnaise were added, giving an additional 258 g fat and 10·2 MJ. The four day dietary period was composed of one menu which was repeated each day, whereas two slightly different menus were used alternately during the 14 day diets to facilitate compliance by the subjects. The meals were prepared in the hospital and consumed by the subjects under close supervision.

Subjects were not allowed to drink alcohol throughout the study periods but were allowed to consume a maximum of three 300 ml glasses of water a day. Daily exercise was recorded and repeated at similar times during their second dietary period.

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TABLE I *Standard diet consumed by subjects each day on the low fat diet (+ indicates the additions to this diet to constitute the high fat diet)*

Breakfast (carbohydrate 137·7 g, fat 2·38 g, protein 21 g, 2·5 MJ):
50 g Cornflakes (Martins)
200 ml skimmed milk (Long Life, Super Low)
3 medium slices toast (Homepride)
54 g marmalade (Margetts)
cup coffee – 50 ml skimmed milk

Lunch (carbohydrate 136 g, fat 6·4 g, protein 31 g, 2·98 MJ):
4 medium slides bread (Homepride)
*113 g onion and chive cottage cheese (Shape)
60 g cucumber
100 g lettuce
130 g tomatoes
190 g new potatoes (Presto)
Half egg yolk, 0·2 g mustard, 20 ml vinegar
40 g apple
36 g boiled sweets
cup coffee, 50 ml skimmed milk

Tea (carbohydrate 95 g, fat 2·2 g, protein 64 g, 2·78 MJ):
1 oxo, 350 ml water
*180 g cod (Birds Eye)
*200 g cauliflower (Presto)
100 g peas (Birds Eye)
100 g tomatoes
300 g potatoes
*Sauce – 10 g cornflour, 100 ml skimmed milk, 2 g chives
*Low fat strawberry yoghurt (Shape)
1 cup coffee, 50 ml skimmed milk

Supper (carbohydrate 43·5 g, fat 0·4 g, protein 1·6 g, 0·71 MJ):
40 g apple
34 g boiled sweets
cup coffee – 50 ml skimmed milk

Total: 9·1 MJ, 121·7 g protein, 419·27 g carbohydrate, 11·6 g fat (additional fat on high fat diet 258 g, 10·2 MJ)

*These items were replaced for the 14 day diet by: 100 g lean turkey breast; 200 g lean beef; 200 g broccoli; sauce: half oxo cube, 10 g cornflour, 100 ml water; banana flavoured yoghurt, respectively (total 8·98 MJ for the low fat diet).
+the addition of 200 g butter and 100 g mayonnaise and the substitution of skimmed milk for full cream milk gives an additional 258 g (10·2MJ) of fat; these items were not included in high fat diet since already in mayonnaise.

MEASUREMENT OF GASTROINTESTINAL TRANSIT

After a 12 hour overnight fast and between 9 30 and 10 am each subject was placed in a semi-recumbent position under the head of an anteriorly placed gammacamera (Model 1201 Pho/Gamma Scintillation Camera; Nuclear Chicago), which was linked to a dedicated minicomputer. Subjects then ate a test meal, consisting of 300 g reconstituted mashed potato containing 68·3 g powdered mashed potato (0·91 MJ), 170 ml water, and 60 g butter plus 160 g baked beans (Crosse and Blackwell, Croydon, Surrey) (0·49 MJ). A radioactive marker (1·85 MBq ^{99m}Tc-Tin colloid (Amersham International, Bucks, UK) was incorporated into the water that reconstituted the mashed potato.

Images of the distribution of radioactivity in the abdomen were collected at intervals of two minutes for a total of 150 minutes and stored on magnetic disc. When the data were replayed a region of interest was drawn around the stomach, which could be easily identified in the first few images gathered after ingestion of the meal. The radioactivity in the gastric region of interest was counted in every image and expressed as a percentage of the total number of counts in that region immediately after consumption of the meal. These figures were then used to construct profiles of gastric emptying without knowledge of the phase of the study. The time for half of the test meal to empty from the stomach ($t^1/_2$) and the percentage of the meal remaining in the stomach at 100 minutes were derived from these profiles. Time zero was defined as the time of meal completion.

The mouth to caecum transit time of the head of the test meal was measured at the same time as the determination of gastric emptying by breath hydrogen analysis.[16] End expiratory breath samples were collected into 50 ml syringes from a modified Haldane-Priestly tube[17] before ingestion of the test meal and at 10 minute intervals thereafter until a sustained increase of at least 10 ppm above basal values was obtained. The hydrogen concentration in these samples was measured using an exhaled hydrogen monitor (GMI Medical Limited, Renfrew). The mouth to caecum transit time of the head of the test meal was taken as the time from ingestion of the meal to a rise of 3 ppm above basal values which was maintained or increased over the next two consecutive 10 minute readings.[18]

SATIETY MEASUREMENTS

At 7 00 pm on the same day subjects were served a preselected appetising two course meal in quantities in excess of what they would normally eat.[19] Orange squash was provided to drink with the meal. The only other meal they had eaten that day was the test meal used to measure gastrointestinal transit time, which was consumed at 10 am. The purpose of this regimen was to gain information about possible long term adaptations of eating behaviour that were unaffected by differences in the composition of the previous meal.[20]

The subject ate the meal by himself in a relaxed and unstressed atmosphere while reading. Subjects scored their subjective feelings of hunger and fullness on a scale of 1 to 10 on visual analogue scales at 10 minute intervals for 30 minutes before and 90 minutes after the start of the meal. The time taken for the subject to complete the meal and the amount of food and drink consumed were measured, and from these figures the rate of ingestion was calculated.

STATISTICAL ANALYSIS

The statistical significance of the differences in the paired observations between the high and low fat dietary regimens were assessed by the Wilcoxon signed rank test and differences between unpaired observations were assessed by the Mann-Whitney U test. Data are expressed as median values and ranges unless otherwise stated.

Results

GASTRIC EMPTYING

There was no significant difference in the half times for gastric emptying after subjects had consumed the high fat or the low fat diets for four days ($t^1/_2$=110·5 (78–143) and 115 (85–145) minutes respectively), though less food was left in the stomach at 100 minutes after consumption of the test meal when subjects were on the high fat diet (50 (33–67) *v* 57 (38–76)%, $p<0·05$) (Fig 1).

When the diets were consumed for 14 days gastric emptying was significantly faster after the high fat diet compared with the low fat diet (Fig

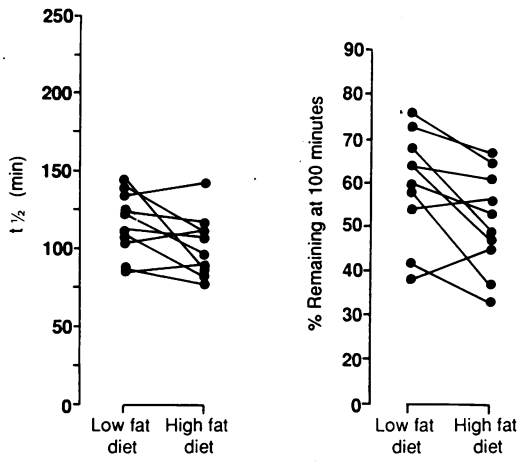

Figure 1: The effect of a low fat diet v a high fat diet, each consumed for four days, on the gastric emptying of a fatty meal.

2) ($t^1/_2$=98 (80–116) *v* 147 (88–206) minutes; p<0·05). There was significantly less food left in the stomach at 100 minutes (50.(36–64) *v* 55% (42–69), p<0·05). There was no significant difference in gastric emptying between the four and 14 day diets.

MOUTH TO CAECUM TRANSIT TIME

There was no significant difference in mouth to caecum transit time after subjects had consumed the high fat or low fat diets for four days (279 (190–368) *v* 275 (180–370) minutes respectively). Consumption of the high fat diet for 14 days, however, resulted in an appreciably shorter transit time than consumption of the low fat diet (240 (130–350) *v* 360 (200–520) minutes, p<0·05) (Figs 2 and 3).

BODY WEIGHT

Body weight was almost identical to what it was at the beginning of the study after consumption of the low fat diet for 14 days (mean (SEM) 72·2 (1·4) *v* 72·7 (1·6) kg), but was significantly higher after a similar period of high fat consumption (74·7 (1·3) *v* 72·7 (1·6) kg; p<0·05).

SATIETY

There were no significant differences in the amounts of food or drink consumed during the two course appetising meal after each of the dietary regimens, although subjects ate more slowly and took longer to consume the meal after they had been on the high fat diet (Table II).

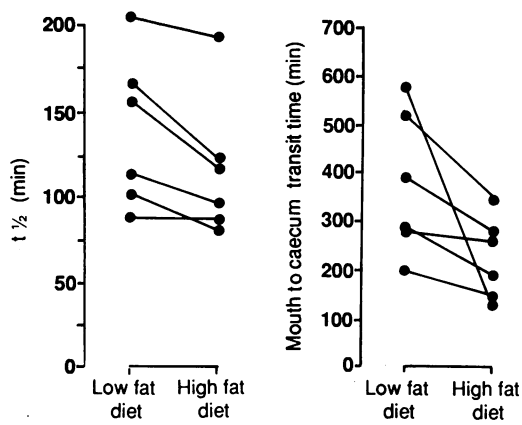

Figure 2: The effect of a low fat diet v a high fat diet, each consumed for 14 days, on the time taken for a fatty test meal to empty by 50%, and the small bowel transit time is shown.

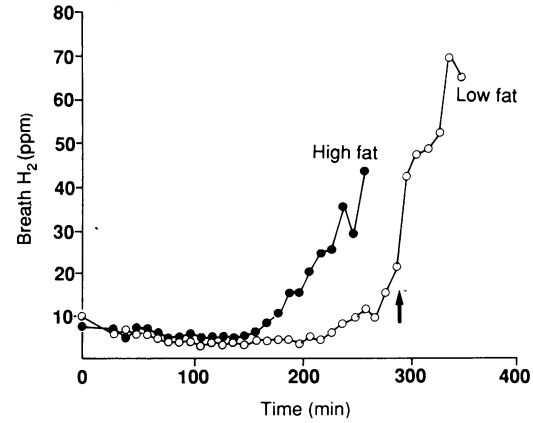

Figure 3: A typical example showing the effect of a low fat v a high fat diet, when consumed for 14 days, on mouth to caecum transit time (minutes).

TABLE II *Effect of a high fat v a low fat diet, each consumed for 14 days, on feeding behaviour and satiety (Mean (SEM) given)*

	High fat	*Low fat*	*p*
Amount eaten (g)	1551·8 (150·5)	1598·8 (202·4)	NS
Amount drunk (g)	481·8 (85·3)	486·7 (109·5)	NS
Time taken to eat (min)	33·3 (3·1)	24·8 (3·4)	<0·05
Total energy intake (MJ)	11·6 (0·69)	12·2 (0·94)	NS
Eating rate (min)	46·7 (1·9)	71·3 (14·8)	<0·05
Drinking rate (min)	15·4 (3·5)	23·4 (8·1)	NS

NS=not significant.

Drinking rates were not significantly different. Feelings of hunger before the meal and fullness afterwards were similar irrespective of the subjects' recent dietary history.

Discussion

Our results show that both gastric emptying and mouth to caecum transit time are significantly faster after a 14 day period on a high fat diet than after 14 days on a low fat diet. Similar but less pronounced effects on gastric emptying but not small bowel transit time were seen after the four day diet. The meal was observed to enter the duodenum in the first five minutes after completion of the meal; therefore, the measurement of mouth to caecum transit time should provide a useful index of small bowel transit time.

The changes observed in gastrointestinal transit would support the hypothesis that small intestinal regulatory mechanisms had been desensitised by a period of exposure to large amounts of fat and sensitised by exposure to relatively small amounts of fat. As such, they emphasise the importance of the recent dietary history in interpreting measurements of gastric emptying. Similar, but less pronounced effects on gastric emptying but not small bowel transit time were seen after four days' dietary exposure to fat.

The mechanism underlying the adaptive responses could be mediated by changes in receptor density, though the existence of specific intestinal receptors for fats is not established. Alternatively, the adaptive responses could be

related to release or sensitivity to humoral transmitters. If so, cholecystokinin and peptide YY might be prime candidates since they have been shown to be released by the presence of fat products in the small intestine[21 22] and can delay gastric and small intestinal transit.[23-26] Obese rats show a decreased sensitivity to cholecystokinin,[27] and it has been proposed that this may be a consequence of increased meal size.[28]

Another possibility is that motor adaptation might be mediated by decreases in the area of the small intestine exposed to the fat in the test meal. Increasing the nutrient content of the diet is known to cause adaptive increases in small intestinal cell proliferation,[29] small intestinal length,[30] and nutrient uptake.[31 32] Thus subjects adapted to high fat intake would be expected to absorb a test meal in the upper small intestine more efficiently than subjects maintained on a low fat diet. This could result in a reduced intestinal field of receptors activated by fat in the test meal and diminished exposure of fat to the powerful ileal mechanisms that slow gastric emptying and small bowel transit.[33] The observation that small bowel transit is delayed by infusion of lipid in the ileum but not the jejunum would support this hypothesis. In experiments on dogs equipped with small intestinal fistulas Lin *et al* have recently shown that the most important factor in the inhibition of gastric emptying by intestinal glucose is the receptor field exposed to the stimulus.[34] Finally, we cannot rule out possible mediation by a non-specific change in caloric intake or other metabolic factors related to weight gain.

Exposure to a high fat diet over two weeks did not result in any change in the amount of a test meal consumed or feelings of hunger before and after the meal, though it was associated with a slower rate of eating. This result was a surprise since from our previous work[19 20] we had expected that desensitisation of lipid receptors might enhance the capacity for a meal and increase the rate of eating. It is possible that carrying out a test at the end of the day during which the subject had remained in the laboratory and consumed only one meal (the test meal) had caused psychological feelings of hunger to override possible physiological mechanisms.

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